CLAIMS

1. A method of stabilising the native state of a polypeptide, the method comprising exposing the polypeptide to a stabilising molecule that binds to the polypeptide at a site which at least partially overlaps a functional site in the native state of the polypeptide.

2. The method of Claim 1, in which the polypeptide is reversibly denatured such that it exists in a native state and a denatured state, in which the stabilising molecule does not bind to the polypeptide in its denatured state.

3. A method of increasing the concentration of a native state of a reversibly denatured polypeptide in a system, in which the system comprises the polypeptide in a first, native state and a second, denatured state, the method comprising:

(a) providing a stabilising molecule which binds to the polypeptide at a site which at least partially overlaps with a functional site in the first native state and thereby stabilising the first, native state of the polypeptide; and

(b) contacting the stabilising molecule with the polypeptide, whereby the concentration of the polypeptide in its native state is incresased.

4. A method of restoring a wild-type phenotype of an organism comprising a mutation in a polypeptide, in which the mutation results in denaturation of the polypeptide and a mutant phenotype, the method comprising exposing the organism or part of the organism to a stabilising molecule which binds to the polypeptide in its native state at a site which at least partially overlaps a functional site of said polypeptide and thereby stabilises the native state of the polypeptide.

5. A method of treatment of a disease in a patient, in which the disease is caused by or associated with a mutation in a polypeptide which results in denaturation of the polypeptide, the method comprising administering to the patient a stabilising molecule which binds to the polypeptide at a site which at least partially overlaps a functional site in its native state and thereby stabilises the native state of the polypeptide.

6. The method of claim 1, in which the stabilising molecule is not a natural binding partner of the polypeptide.

7. The method of claim 1, in which the stabilising molecule consists of a fragment of a natural binding partner of the polypeptide.

8. The method of claim 1, in which the stabilising molecule is a polypeptide engineered to include a polypeptide binding domain of a natural binding partner of the polypeptide.

9. The method of claim 8 wherein said polypeptide binding domain is a binding loop of said natural binding partner of said polypeptide.

10. The method according to claim 1, in which the stabilising molecule is exposed to the polypeptide in presence of a natural binding partner of the polypeptide.

11. The method of claim 1, in which the affinity of binding between stabilising molecule and the polypeptide or site is less than the affinity of a natural binding partner of the polypeptide and the polypeptide or the binding site.

12. The method of claim 1, in which binding between the stabilising molecule and the binding site stabilises the polypeptide and thereby permits binding between the polypeptide and a natural binding partner.

13. The method of claim 1, in which binding between the polypeptide and a natural binding partner stabilises the native state of the polypeptide.

14. A method of assisting the binding between a polypeptide and a natural binding partner for the polypeptide, the method comprising stabilising a native state of the polypeptide by a method according to claim 1, and exposing the stabilised polypeptide to the natural binding partner, wherein binding of the polypeptide to the natural binding partner is assisted.

15. A method of assisting the binding between a polypeptide and a first molecule, in which the polypeptide exists in a native state and a denatured state, the method comprising:

(a) providing a second stabilising molecule that binds to a site which at least partially overlaps a functional site in the native state of the polypeptide;

(b) permitting the second stabilising molecule to bind to the polypeptide to form a complex, thereby stabilising the native state of the polypeptide;

(c) exposing the polypeptide and bound second stabilising molecule complex to the first molecule; and

(d) permitting the first molecule to bind to the polypeptide and thereby displacing the second stabilising molecule, wherein binding between the polypeptide and the first molecule is assisted.

16. The method of claim 1, 14 or 15, in which the functional site comprises or at least partially overlaps with a structural domain, a protein binding domain, a nucleic acid binding domain, or an active site of an enzyme.

17. The method according to Claim 15, in which the functional site is essential to the structure or activity, or both, of the polypeptide.

18. The method according to claim 1, 14 or 15, in which the polypeptide comprises an oncogenic protein or a tumour suppressor protein.

19. The method according to claim 18, in which the polypeptide is p53.

20. The method of claim 18, in which the polypeptide is p53 which comprises a mutation, selected from R175H, G245S, R248Q, R249S, R273H, R282W and I1951, which mutation results in reversible denaturation of the polypeptide.

21. The method of any one of claims 1, 14 and 15, in which the stabilising molecule comprises a CDB3 polypeptide having the sequence REDEDEIEW.

22. The method of any one of claims 1, 14 and 15 wherein said stabilising molecule comprises an organic or inorganic small molecule, a natural or derivatised carbohydrate, protein,

polypeptide, peptide, glycoprotein, nucleic acid, DNA, RNA, oligonucleotide or protein-nucleic acid (PNA).

23. The method of claim 22 wherein said stabilising molecule is derivatised with a sugar, phosphate, amine, amide, sulphate, sulphide, biotin, a fluorophore or a chromophore.

24. A stabilising molecule which binds to and stabilises the native state of a polypeptide, but not a denatured state of the polypeptide, in which the stabilising molecule binds to a site which at least partially overlaps a functional site of the polypeptide, and in which the stabilising molecule does not consist of a natural binding partner of the polypeptide.

25. The stabilising molecule of Claim 24, in which the polypeptide is p53.

26. The stabilising molecule of Claim 25, in which the polypeptide is p53 which comprises a mutation, selected from R175H, G245S, R248Q, R249S, R273H, R282W and I195T in which the mutation results in reversible denaturation of the polypeptide.

27. The stabilising molecule of Claim 24, in which the stabilising molecule comprises a CDB3 polypeptide having the sequence REDEDEIEW.

28. The stabilising molecule of claim 24, wherein said molecule comprises an organic or inorganic small molecule, a natural or derivatised carbohydrate, protein, polypeptide, peptide, glycoprotein, nucleic acid, DNA, RNA, oligonucleotide or protein-nucleic acid (PNA).

29. The stabilising molecule of claim 28 wherein said molecule is derivatised with a sugar, phosphate, amine, amide, sulphate, sulphide, biotin, a fluorophore or a chromophore.

30. A method of identifying a stabilising molecule that stabilises a polypeptide, the polypeptide is reversibly denaturable such that it exists in a native state and a denatured state, the method comprising the steps of:

(a) providing a native state of the polypeptide comprising a functional site;

(b) exposing the polypeptide to a candidate stabilising molecule;

(c) selecting a candidate stabilising molecule which binds to a site which at least partially overlaps said functional site of the native state of the polypeptide; and

(d) determining whether such binding stabilises the native state of the polypeptide.

31. A method of identifying a stabilising molecule that stabilises a polypeptide, wherein the polypeptide is reversibly denaturable, such that it exists in a native state and a denatured state, the method comprising the steps of:

(a) identifying a functional site of the polypeptide and providing a polypeptide fragment comprising the functional site;

(b) selecting a candidate stabilising molecule which binds to the polypeptide fragment at a site which at least partially overlaps said functional site; and

(c) determining whether the selected candidate stabilising molecule stabilises a native state of the polypeptide.

32. The method of claim 30 or 31 wherein said stabilising molecule comprises an organic or inorganic small molecule, a natural or derivatised carbohydrate, protein, polypeptide, peptide, glycoprotein, nucleic acid, DNA, RNA, oligonucleotide or protein-nucleic acid (PNA).

33. The method of claim 32 wherein said stabilising molecule is derivatised with a sugar, phosphate, amine, amide, sulphate, sulphide, biotin, a fluorophore or a chromophore.

34. The method of claim 31, in which the polypeptide fragment comprising the functional site includes a binding site for a natural binding partner of the polypeptide.

35. A method of claim 22 in which the stabilising molecule is derivatised with a fluorophore.

36. A method of claim 32 in which the stabilising molecule is derivatised with a fluorophore.

37. The methods of claim 35 wherein said stabilising molecule is derivatised with fluorescein.

38. The methods of claim 36 wherein said stabilising molecule is derivatised with fluorescein.

39. The stabilising molecule of claim 24 in which the stabilising molecule is derivatised with a fluorophore.

40. The stabilising molecule of claim 39 wherein said fluorophore is fluorescein.

41. The method of any one of claims 1, 14, 15, 30, or 31, further comprising detecting the binding of a stabilising molecule to the polypeptide using NMR spectroscopy, fluorescence anisotropy, surface plasmon resonance, or Differential Scanning Calorimetry (DSC).

42. A method of treating a disease, the method comprising administering a therapeutic amount of a stabilising molecule of claim 24 to an individual, wherein said disease is treated.

43. The method of claim 5 or 40 wherein the disease is cancer.

44. A pharmaceutical composition comprising a stabilising molecule according to claim 24, together with a pharmaceutically acceptable carrier, diluent or excipient.

45. A pharmaceutical composition comprising a CDB3 polypeptide having the sequence REDEDEIEW together with a pharmaceutically acceptable carrier, diluent or excipient.

46. A method for inducing the onset or progression of apoptosis in one or more cells comprising the step of contacting those one or more cells with a stabilising molecule of claim 24.

47. The method of claim 44 wherein the stabilising molecule is CDB3 peptide.